

### **REMARKS**

The Office Action of April 11, 2006 presents the examination of claims 1-3, 5-8, 10-11 and 13-26. The present paper amends claims 19 and 21. Claims 1-3, 5-8 and 13-20 presently stand withdrawn from consideration.

Claim 19 is amended to correct improper dependency.

Support for the amendment to claim 21 can be found at page 18, second paragraph of the present specification. The Examiner should note that this portion of the specification includes some description of a "crude particle."

#### **Status of claims**

The Office Action summary fails to indicate the status of claims 10-11. Applicants' Representative notes that claims 10-11 are presently withdrawn from consideration.

#### **Substance of interview**

An interview with the Examiner was held on August 23, 2006. The legal burden borne by Applicants to demonstrate patentable distinction over prior art alleged to anticipate product-by-process claims was discussed. Applicants' Representative pointed out that the burden was to show by a preponderance of the evidence some sort of distinction, be it structural, functional or in some physical characteristic, in the product made by the steps recited in the claim compared to a product made as in the prior art reference. Applicants' Representative further pointed out the Declaration evidence of record of distinctions in particle size distribution and emulsion stability obtained using the process of the present invention, in which an organic solvent is used in the step of dispersing the BCG-CWS component prior to addition of the aqueous phase and emulsifying, compared to a process in which such organic solvent was lacking. Applicants' Representative notes that a common feature of all of the processes of the references cited as anticipating the present claims 21-26 is lack of any organic solvent in the step of dispersing the BCG-CWS prior to addition of the aqueous phase and emulsifying.

A mistake of the Examiner is interpreting the Cantrell '611 reference was also discussed, as explained further below.

#### Rejections over prior art

The issues precluding allowance of the present claims 21-26 relate to rejections over prior art. The rejections of record, which have all been maintained, are as follows:

Claims 21 and 23-26 stand rejected under 35 U.S.C. § 102(b) as lacking novelty over Yamamura, Cantrell or Yarkoni. Claims 21-26 stand rejected under 35 U.S.C. § 102(b) as lacking novelty over Van Nest. Claims 21, 23, 24 and 26 are newly rejected under 35 U.S.C. § 102(b) as lacking novelty over Zbar et al.

All of these rejections are respectfully traversed. Reconsideration and withdrawal thereof are requested.

Applicants have explained in detail that the record already includes sufficient evidence that the process steps recited in the instant claims 21-26 provide a product that is distinct from that obtained by the processes described by Yamamura, Cantrell, Yarkoni, Van Nest or Zbar. In this regard, the Examiner should once again review Applicants' position as set forth in their paper filed February 2, 2006 and the more legible copies of the Declarations relied upon therein left with the Examiner on November 29, 2005. Applicants maintain their view that the explanations provided previously are sufficient to establish patentability of the present invention over the references cited to date.

In particular, Applicants reiterate that the Declaration evidence of previously of record establishes that failure to include an organic solvent in the step of dispersing the CWS component in oil results in the appearance of very large particles in the resulting emulsion, and that the resulting emulsion has a lower stability. On the other hand, if the organic solvent is included as described in the present claims, the resulting emulsion is free of large particles (i.e. particles over 100  $\mu\text{m}$  in diameter as shown in e.g. Figures 1 and 2 of the specification), and the emulsion is stable for a longer time.

Nonetheless, Applicants provide attached further Declaration evidence in the form of additional experiments which seek to compare the product of the invention, i.e. the one obtained using the process steps recited in the present claim 21, with the product obtained by the processes described in the references cited by the Examiner. The attached Declaration of Dr. Norimasa Koseki provides explanation of experiments were conducted on the basis of disclosure in the Yamamura et al. and Zbar et al. references, and his conclusions regarding the product obtained compared to the product obtained using the process recited in the present claim 21. Applicants note that the attached copy of the Koseki Declaration includes data in the form of color photographs, which unfortunately are not very clear. Applicants' Representative will be filing an original copy of the Declaration having clear photographs in a Supplemental Response as soon as such copy is received.

Dr. Koseki's Declaration presents the following experiments:

Experiment 1 shows that the paste of BCG-CWS and an oil, which is the starting material for emulsification, obtained according to the method of Yamamura (Example 1) or Zbar (Experiment) was not suitable for preparing a good emulsion. In particular the pastes resulting from the oiling steps of Yamamura or Zbar do not adequately coat the powdered CWS material to provide a sufficient dispersion (i.e. a homogeneous dispersion, see page 17, lines 10-24, of the specification). On the other hand, using an organic solvent as in the present invention, the oil is sufficiently dispersed over the CWS to completely cover it.

Experiments 2 and 3 show the preparation of emulsion according to the methods of Yamamura (Example 1) and Zbar (Experiment), respectively. The results are shown in Figs. 3 and 4, respectively.

#### Emulsion of the Present invention

Figure 5 shows an emulsion of the present invention for comparison.

The details of the experiments and the results (Dr. Koseki's observations) are set forth in his Declaration. The Examiner should note that the preparations made according to Yamamura

and Zbar do not provide uniform emulsions. Instead, there are large amounts of the BCG-CWS that remain un-emulsified. On the other hand, the emulsion prepared by the steps recited in the present claim 21 is uniform.

Discussion of each of the cited references in relation to the evidence provided by Dr. Koseki's Declaration follows.

*Yamamura et al.*

Yamamura et al. discloses only N. rubra-CWS specifically, although the reference also includes description of a composition containing BCG-CWS, Squalene and Tween.

In the previously filed Nomura Declaration II, Applicants conducted a comparative experiment using BCG-CWS together with Squalene and Tween to obtain a composition which is close to the composition of the present invention. The N. rubra-CWS of Yamamura was hardly available. The product prepared without using an organic solvent indeed contained huge particles as shown in Declaration II. On the contrary, the composition of the present invention did not contain any particles of 25  $\mu\text{m}$  or larger. Therefore, the present invention is patentably distinct from the composition disclosed in Yamamura et al.

In addition, the product obtained according to the method described in Yamamura et al. did not form a "uniform emulsion," as shown in the Experiment 2 and Fig. 3 of Dr. Koseki's Declaration.

*Yarkoni et al.*

The composition disclosed in Yarkoni et al. is the same as the one disclosed in Yamamura et al., and thus Applicants' prior arguments and the additional comparative evidence of the Koseki Declaration apply as well to Yarkoni et al.

*Zbar et al.*

As Applicants have explained previously, Zbar et al., as all of the presently cited references, do not disclose a process for preparing an emulsion of CWS that includes a step of dispersing the CWS in oil using an organic solvent prior to the adding of the aqueous phase and emulsifying. The resulting product is therefore not expected to form a stable, uniform emulsion as shown by the previous evidence of record. This expectation is realized, as the product obtained according to the method described in Zbar et al. did not form a uniform emulsion, as shown in Experiment 3 and Fig. 4 of the attached Declaration of Dr. Koseki.

*Cantrell et al.*

Cantrell et al., like all of the other references cited, does not disclose use of any organic solvent at the step of dispersing the CWS component in an oil. The Examiner has asserted to the contrary that Cantrell et al. do disclose use of an organic solvent in the making of an emulsion, citing col. 9 of the patent.

As explained in the interview of August 23, 2006, this portion of Cantrell describes purification of trehalose-mycolate (TDM), which is a sugar substance, not preparation of CWS. TDM and CWS are distinct materials, as evidenced by the listing of them separately in Table 7 in Example 11. Even if TDM is deemed equivalent to CWS, the text cited indicates that after the extraction with organic solvent, further purification by chromatography is described, without indication whether the product is eluted in an organic solvent or in an aqueous phase. Thus, the resulting TDM material is taken to be free of organic solvent prior to use in the preparation of an emulsion.

Accordingly, Cantrell et al. do not disclose any method for preparing an emulsion of CWS as in the present invention, and the emulsion expected to result is one that is different from that of the present invention, as well-established by the evidence of record in this matter.

*Van Nest et al.*

As explained previously, Van Nest et al. do not disperse a BCG-CWS component in an organic solvent and oil prior to adding an aqueous phase and emulsifying. See, Example 1 at column 13. Furthermore, Van Nest et al. do not utilize BCG-CWS in their preparation at all. Rather, Van Nest et al. use MTP-PE (muramyl tripeptide-phosphatidylethanolamine, col. 2, line 22). Thus, Van Nest et al. is entirely distinct from the present invention.

Applicants submit for the above reasons that the present invention as set forth in claims 21-26 is novel over each of Yamamura, Yarkoni, Cantrell, Zbar and Van Nest. Accordingly, all of the standing rejections should be withdrawn.

In view of the above amendment, applicant believes the pending application is in condition for allowance and such favorable action is respectfully requested.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Mark J. Nuell Reg. No. 36,623 at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

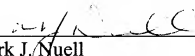
Application No. 09/743,750  
Amendment dated October 11, 2006  
After Final Office Action of April 11, 2006

Docket No.: 0020-4802P

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§1.16 or 1.14; particularly, extension of time fees.

Dated: October 11, 2006

Respectfully submitted,

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Attachment: Declaration Under 37 C.F.R. § 1.132 by Dr. Norimasa Koseki